PEGGY GREB (K9831-1)

# Baby's Weight: Is Epigenetics To Blame?

**Findings by ARS scientists may underscore the need for aspiring moms to achieve a healthy weight before becoming pregnant and to gain only the recommended amount of weight during pregnancy.**

No one is surprised when the child of an overweight mother becomes overweight or even obese. But scientists at two ARS-funded nutrition research centers are taking a new and closer look at how influences occurring in the womb and perhaps during the first few months of life might affect development of the child's ability to regulate his or her weight. The child's body-weight-regulating mechanisms might in fact be harmed during those times by the mother's own overweight.

Such maternal programming of the unborn child and the developing newborn could increase the risk that the child would become an overweight or obese adult. In turn, that adult would have a higher risk of obesity-related afflictions such as type 2 diabetes or cardiovascular disease.

Understanding more about little-known heritable maternal influences may lead to new ways to help at-risk youngsters keep excess pounds at bay.

Kartik Shankar, an investigator with the ARS Arkansas Children's Nutrition Center in Little Rock and an assistant professor of pediatrics at the University of Arkansas for Medical Sciences, looked at weight gains among rat pups whose mothers, called "dams," were either lean or overweight (from overfeeding) at the time of conception and during pregnancy.

For this research, Shankar and colleagues mated the lean or overweight female rats with lean males. The pups were nursed only by normal-weight dams "to make sure that the pups' exposure to their mother's obesity occurred only in the womb," Shankar says.

All pups were of normal weight at birth and at weaning. However, when the weaned offspring were given free access to an unlimited amount of high-fat rations, the offspring of overweight dams gained significantly more weight, and more of that weight as fat, than did the offspring of lean dams.

"This occurred despite the fact that the offspring of overweight dams ate the same amount of high-fat food as the offspring of lean dams," Shankar points out.

"Our study strongly suggests that exposure to the mother's obesity—while in the womb—results in programming of the offspring's body-weight-control mechanisms," he says. "The dams' obesity alone was sufficient to significantly increase the pups' susceptibility to obesity."

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**Kartik Shankar, an investigator at the ARS Arkansas Children's Nutrition Center in Little Rock, analyzes rat fat cells. The size of fat cells in offspring is influenced by maternal obesity.**

Since Shankar's group used only rats that were genetically similar, the scientists essentially ruled out the possibility that any important genetic differences among the dams could contribute to the remarkable difference in pups' sensitivity to the high-fat rations.

If proven true for humans, the findings would underscore the need for aspiring mothers to achieve a healthy weight before becoming pregnant and to gain only the recommended amount of weight during their pregnancy. Right now, the incidence of overweight or obesity among pregnant women in America continues to increase, according to Shankar.

His team documented this study in a 2008 article in the *American Journal of Physiology–Regulatory, Integrative and Comparative Physiology.*

Maternal obesity may alter pups' body-weight-controlling mechanisms in a way not described by traditional Mendelian genetics. Instead, this programming may result from what's known as an "epigenetic mechanism."

Literally translated, epigenetics means "on or above genetics." When an epigenetic mechanism is in play, genes themselves aren't altered. But the way the genes function, or are "expressed" (turned on or tuned off), during early growth is indeed changed.

Once highly controversial, epigenetics has at least won some acceptance as having a role in human disease, in part because of increasing evidence of epigenetic linkages to cancer.

Epigenetics may provide the explanation for an obesity phenomenon described in a 2008 study led by Robert A. Waterland. He's conducting follow-up research in his laboratory at the ARS Children's Nutrition Research Center at Baylor College of Medicine in Houston, Texas, where he is an assistant professor of pediatrics.

Waterland did the research with a population of genetically similar laboratory mice known for their genetic tendency toward obesity. He says the findings suggest that "an epigenetic mechanism may act to increase the severity of obesity from one generation to the next."

This "transgenerational amplification of obesity" occurred in three successive generations of mice that Waterland and coinvestigators studied. Specifically, overweight dams gave birth to even-more-overweight offspring, the females of which gave birth to even heavier pups, and so on, through generation three.

Reported in the *International Journal of Obesity,* the study showed that the mothers' obesity apparently induced changes in the expression of genes that control the formation of the pups' body-weight-regulating mechanisms. That likely took place in the womb and perhaps in the weeks thereafter, setting the pups on the path to obesity.

Scientists elsewhere have shown that effects resulting from an epigenetic mechanism might be reversed in lab animals by feeding them rations that boost an epigenetic process known as "DNA methylation." That appears to be what happened when Waterland and colleagues provided dams with methylation-enhancing chow. That's a research procedure, not a cure for obesity, Waterland cautions.

Right now, these leading-edge investigations into mother's overweight and baby's epigenetically controlled predisposition to obesity perhaps raise more questions than they answer. But the studies provide a strong foundation for new research that might help to unburden tomorrow's generations from a lifelong struggle with obesity.—By **Marcia Wood,** ARS.

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